Biochemical Research Laboratory
THE DOW CHEMICAL COMPANY

Subject: RESULTS OF RANGE FINDING TOXICOLOGICAL STUDIES ON SOME OF THE DOWANOLS

Distribution

Rept. By V. K. Rowe 10-23-47

PROBLEM

Some of the Dowanols, particularily the mono-methyl and mono-butyl ethers of propylene, dipropylene, and tripropylene glycols are of particular interest to The Dow Chemical Company. Toxicological information regarding these materials was desired as a guide to developmental work being carried out by the Technical Service and Development Division. Toxicological information on the ethyl and methyl ethers of ethylene and diethylene glycol was also desired for comparative purposes.

MATERIAL

The materials covered in this report were all supplied by Mr. J.C. Moore of 258 Lab. They are described below in Table I.

TABLE I

Dowanol No.	Name Glycol, Mono Alkyl ether	Drum	Empirical Formula	B P °C at 760 mm Hg.
7	E.G., Methyl	56	$C_3H_8O_2$	122.5
8	E.G., Ethyl	51	$C_4H_{10}O_2$	134.6
16	Di-E.G., Methyl	57	$C_5H_{12}O_3$	194.
17	Di-E.G. Ethyl	52	$C_6H_{14}O_3$	201

Dowanol No.	Name Glycol, Mono Alkyl ether	Drum #	Empirical Formula	B P °C at 760 mm Hg
33B	P.G., Methyl	85	$C_4H_{10}O_2$	119.2
37B	P.G., n-Butyl	2	$C_7H_{16}O_2$	169.8
50B	Di-P.G., Methyl	95	$C_7H_{16}O_3$	189
54B	Di-P.G., n-Butyl	3	$C_{10}H_{22}O_3$	228
62B	Tri-P.G., Methyl	16B	$C_{10}H_{22}O_4$	242
66B	Tri-P.G., n-Butyl	30	$C_{13}H_{28}O_4$	?

EXPERIMENTAL

Acute Oral - The undiluted materials were fed to rats in single oral doses. The results are given below in Table II.

TABLE II

Dowanol No.	Largest Dose Survived by All 5 Rats Fed ml/kg	Smallest Dose Causing Death in All 5 Rats fed. ml/kg	Estimated LD_{50} (our work) ml/kg	LD_{50} from literature g/kg or ml/kg
7	1.0	3.0	2-3	2.46 (1)
8	2.0	5.0	2.5-3.5	3.00 (1) 3.46 (2)
16	2.0	10.0	4-5	9.21 (1)
17	3.0	6.0	4-5	9.74 (1) 5.54 (2)
33B	5.0	10.0	7.5-8.5	7.51 (1)
37B	1.0	3.0	2-3	
50B	3.0	7.0	5.5-6.5	
54B	1.0	3.0	2-3	
62B	1.0	7.0	3.5-4.5	
66B	1.0	5.0	2-3	

(1) Expressed as g/kg - See Ref. No. 1
(2) Expressed as ml/kg - See Ref. No. 2

These figures show quite conclusively that when given to rats in single oral doses: (1) Dowanol 33B is less toxic than any of the other materials tested; and (2) the methyl ethers of the propylene glycols are distinctly less toxic than the corresponding butyl ethers.

It is interesting to note that our figures (LD_{50}) for the methyl and ethyl ethers of diethylene glycol are considerably lower than those of Smith, et al (1) and quite similar to those of Laug, et al (2) of the F.D.A. A satisfactory explanation of these apparent discrepancies is lacking particularily when it is noted that our figures (LD_{50}) for the methyl and ethyl ethers of ethylene glycol are essentially the same as those reported by Smith (1).

Eye and Skin Irritation - All of this group of materials except Dovanols 7 and 8 have been tested for eye and skin irritation. In each case the undiluted material was dropped into the rabbit eye daily for 5 days and applied repeatedly to the rabbit ear and belly (10 times in 2 weeks).

As far as eye irritation was concerned, the materials can be divided into 3 groups: Dovanols 16,17, and 66B failed to cause more than a mild immediate irritation; Dovanols 33B, 50B, 54B, and 62B all produced some conjunctival irritation very apparent after 24 hours but probably not of lasting character; Dovanol 37B was quite irritating and caused serious effects.

As far as skin irritation was concerned, Dovanol 37B was also the most irritating of the group. None of the others produced more than a very slight irritation and Dovanols 16, 17, 33B and 62B were the least irritating of the group.

CONCLUSIONS

The toxicological work so far completed indicates that Dovanol 33B may offer distinct toxicological advantages over the other Dovanols tested. It is the least toxic when given in single oral doses to rats, it is not appreciably irritating to the skin, and even though it is slightly more irritating to the eyes than some of these materials, it is doubtful that this factor will be a significant commerical limitation.

On the other hand, Dowanol 37B appears to be as toxic as any of the group when given orally, and the most irritating to the eyes and th skin. These factors may well serve to limit the applications for which this material is suitable.

Note: Further toxicological studies involving the vapor toxicity and the skin absorption problems of these materials are either underway or will be begun in the near future.

References:

(1) The Single Dose Toxicity of Some Glycols and Derivatives. H.F. Smyth, Jr., Jane Seaton and Louise Fischer Jour. Ind. Hgy. and Tox. 23, No. 6 pg. 259 (1941).

(2) The Toxicology of Some Glycols and Derivatives. E.P. Laug, H.O. Calvery, and H.G. Morris and G. Woodard. Jour. Ind. Hyg. and Tox. 21 No. 5 pg. 173 (1939)

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